

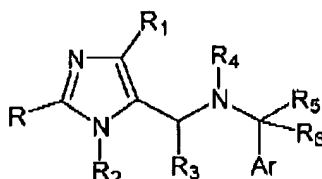
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AMENDMENTS TO THE CLAIMS

1. (Currently Amended) A compound of the formula:



or a pharmaceutically acceptable form thereof, wherein:

R represents:

- (i) hydrogen, halogen, cyano or C₁-C₂ haloalkyl, or
- (ii) C₁-C₄alkyl, C₂-C₄alkenyl, C₂-C₄alkynyl, C₁-C₂alkanoyl, C₃-C₇cycloalkyl, C₃-C₇cycloalkenyl or heterocycloalkyl, each of which is optionally substituted;

R₁ represents:

- (i) hydrogen, hydroxy, halogen, amino, cyano, nitro, C₁-C₂haloalkyl or C₁-C₂ haloalkoxy;
- (ii) C₁-C₄alkyl, C₂-C₄alkenyl, C₁-C₄alkoxy, C₃-C₇cycloalkyl, (C₃-C₇cycloalkyl)C₁-C₂alkyl, or mono- or di-C₁-C₆alkylamino, or
- (iii) phenylC₀-C₄carbhydrl or (5- or 6-membered heteroaryl)C₀-C₄carbhydrl, each of which is optionally substituted;

R₂ is optionally substituted C₁-C₇ alkyl or optionally substituted C₂-C₇ alkenyl;

R₃ is hydrogen or C₁-C₆alkyl;

R₄ represents:

- (i) C₁-C₆alkyl, C₂-C₆alkenyl or C₂-C₆alkynyl, each of which is optionally substituted;
- (ii) optionally substituted arylC₀-C₂alkyl having 1 ring or 2 fused rings; or
- (iii) optionally substituted arylC₁-C₂alkyl, wherein the aryl portion is fused to a 5- to 7-membered saturated or partially unsaturated ring having 0, 1 or 2 ring atoms independently chosen from N, O and S, with remaining ring atoms being carbon; or
- (iv) optionally substituted (4- to 12-membered heterocycle)C₀-C₄alkyl;

R₅ and R₆ are independently chosen from hydrogen and C₁-C₆alkyl; and

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Ar represents:

- (i) optionally substituted aryl having 1 ring or 2 fused or pendant rings; or
- (ii) optionally substituted phenyl fused to a 5- to 7-membered saturated or partially unsaturated ring having 0, 1 or 2 ring atoms independently chosen from N, O and S, with remaining ring atoms being carbon; or
- (iii) ~~optionally substituted heteroaryl having 1 ring or 2 fused or pendant rings, from 5 to 7 members in each ring, and in at least one ring from 1 to 3 heteroatoms independently selected from N, O and S.~~

2. (Currently Amended) A compound or pharmaceutically acceptable form thereof according to claim 1, wherein:

R represents:

- (i) hydrogen, halogen, cyano or C₁-C₂haloalkyl; or
- (ii) ~~G₁-G₄alkyl, G₂-C₄alkenyl, C₂-G₄alkynyl, G₁-C₂alkanoyl, G₃-C₇cycloalkyl, G₃-C₇ cycloalkenyl or 5- to 7-membered heterocycloalkyl, each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, oxo, C₁-C₄alkyl, C₁-C₄alkoxy and C₁-C₂alkoxycarbonyl;~~

R₁ represents:

- (i) hydrogen, hydroxy, halogen, amino, cyano, nitro, C₁-C₂haloalkyl or C₁-C₂ haloalkoxy;
- (ii) C₁-C₄alkyl, C₂-C₄alkenyl, C₂-C₄alkynyl, C₁-C₄alkoxy, C₃-C₇cycloalkyl, (C₃-C₇cycloalkyl)C₁-C₂alkyl, or mono- or di-C₁-C₄alkylamino, each of which is substituted with from 0 to 3 substituents independently chosen from hydrogen, hydroxy, halogen, amino, cyano, oxo, C₁-C₄alkyl, C₁-C₄alkoxy and C₁-C₂alkoxycarbonyl; or
- (iii) phenylC₀-C₄carbhydryl or (5- or 6-membered heteroaryl)C₀-C₄carbhydryl, wherein each 5- or 6-membered heteroaryl is independently chosen from imidazolyl, pyridyl, thiazolyl, pyrrolidinyl and thienyl, and wherein each phenylC₀-C₄carbhydryl or (5- or 6-membered heteroaryl)C₀-C₄carbhydryl is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, nitro, -COOH, -

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CONH₂, -SO₂NH₂, C₁-C₂ haloalkyl, C₁-C₂ haloalkoxy, C₁-C₄ alkyl, C₁-C₄alkoxy, C₂-C₄alkanoyl, C₁-C₂alkylsulfonyl, C₁-C₂alkylsulfinyl and C₁-C₂alkylthio;

R₂ is C₁-C₇alkyl or C₂-C₇alkenyl, each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, oxo, C₁-C₂alkoxy, C₁-C₂ mono- and di-alkylamino, C₃-C₇cycloalkyl and phenyl;

R₃ is hydrogen or C₁-C₆alkyl;

R₄ represents:

~~(i) C₁-C₆alkyl, C₂-C₆alkenyl or C₂-C₆alkynyl, each of which is substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, C₁-C₂alkyl, C₁-C₂alkoxy, or C₁-C₂alkoxycarbonyl;~~

~~(ii)(i) arylC₀-C₂alkyl having 1 ring or 2 fused rings; or~~

~~(iii)(ii) benzyl fused to a 5- to 7-membered saturated or partially unsaturated ring having 0, 1 or 2 ring atoms independently chosen from N, O and S with remaining ring atoms being carbon; or~~

~~(iv) (4- to 12-membered heterocycle)C₀-C₂alkyl;~~

wherein each of (ii) and (iii) ~~-(iv)-~~ is substituted with from 0 to 4 substituents independently chosen from hydroxy, halogen, amino, cyano, nitro, -COOH, -CONH₂, -SO₂NH₂, oxo, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, C₁-C₄alkyl, C₁-C₄alkoxy, mono- and di-(C₁-C₆)alkylamino, C₁-C₄alkanoyl, C₁-C₂sulfonate, C₁-C₂alkylsulfonyl, C₁-C₂alkylsulfinyl, C₁-C₄alkylthio, C₂-C₄alkanone, C₁-C₄alkyl ester, C₁-C₄alkanoyloxy, C₁-C₂alkoxycarbonyl and C₁-C₂alkylcarboxamido; and

Ar represents:

(i) an aryl group having 1 ring or 2 fused or pendant rings; or

(ii) phenyl fused to a 5- to 7-membered saturated or partially unsaturated ring having 0, 1 or 2 ring atoms independently chosen from N, O and S with remaining ring atoms being carbon; or

~~(iii) a heteroaryl group having 1 ring or 2 fused or pendant rings, from 5 to 7 members in each ring, and in at least one ring from 1 to 3 heteroatoms selected from N, O, and S;~~

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each of which is substituted with from 0 to 4 substituents independently chosen from hydroxy, halogen, amino, cyano, nitro, -COOH, -CONH₂, -SO₂NH₂, oxo, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, C₁-C₄alkyl, C₁-C₄alkoxy, mono- and di-(C₁-C₆)alkylamino, C₁-C₄alkanoyl, C₁-C₂sulfonate, C₁-C₂alkylsulfonyl, C₁-C₂alkylsulfinyl, C₁-C₄alkylthio, C₂-C₄alkanone, C₁-C₄alkyl ester, C₁-C₄alkanoyloxy, C₁-C₂alkoxycarbonyl and C₁-C₂alkylcarboxamido.

3. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein R₅ is hydrogen, and R₆ is hydrogen, methyl or ethyl.

4. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein R₁ is phenyl substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, nitro, -COOH, -CONH₂, -SO₂NH₂, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, C₁-C₄alkyl, C₁-C₄alkoxy, C₂-C₄alkanoyl, C₁-C₂alkylsulfonyl, C₁-C₂alkylsulfinyl and C₁-C₂alkylthio.

5. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein R₁ is phenyl substituted with 1 or 2 substituents independently chosen from hydroxy, halogen, amino, cyano, nitro, -COOH, -CONH₂, -SO₂NH₂, C₁-C₂ haloalkyl, C₁-C₂ haloalkoxy, C₁-C₂alkyl and C₁-C₂alkoxy.

6. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2 wherein R₁ is unsubstituted phenyl.

7. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein R₁ is hydrogen, hydroxy, halogen, amino, cyano, trifluoromethyl, pentafluoroethyl, difluoromethyl, trifluoromethoxy or difluoromethoxy.

8. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein R₁ is halogen.

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9. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein R₂ is propyl, butyl, pentyl or 3-methylbutyl.

10. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein R₃ is hydrogen.

11. (Cancelled).

12. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein R₄ is benzyl substituted with from 0 to 4 substituents independently chosen from hydroxy, halogen, amino, cyano, nitro, -COOH, -CONH₂, -SO₂NH₂, oxo, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, C₁-C₄alkyl, C₁-C₄alkoxy, mono- and di-(C₁-C₆)alkylamino, C₁-C₄alkanoyl, C₁-C₂sulfonate, C₁-C₂alkylsulfonyl, C₁-C₂alkylsulfinyl, C₁-C₄alkylthio, C₂-C₄alkanone, C₁-C₄alkyl ester, C₁-C₄alkanoyloxy, C₁-C₂alkoxycarbonyl and C₁-C₂alkylcarboxamido.

13. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein R₄ is benzyl substituted with from 0 to 2 substituents independently chosen from hydroxy, halogen, amino, cyano, -COOH, -CONH₂, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, C₁-C₂alkyl, mono- and di-(C₁-C₂)alkylamino, C₁-C₂alkoxy, C₁-C₂alkanoyl and C₁-C₂alkoxycarbonyl.

14. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein R₄ is benzyl fused to a 5- to 7-membered saturated or partially unsaturated ring having 0, 1 or 2 ring atoms chosen from N, O, and S with remaining ring atoms being carbon, wherein the benzyl fused to a 5- to 7-membered ring is substituted with from 0 to 4 substituents independently chosen from hydroxy, halogen, amino, cyano, -COOH, -CONH₂, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, C₁-C₂alkyl, mono- and di-(C₁-C₂)alkylamino, C₁-C₂alkoxy, C₁-C₂alkanoyl and C₁-C₂alkoxycarbonyl.

15. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein R₄ is benzo[1,3]dioxol-5-ylmethyl, 2,3-dihydro-1-benzofuran-

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6-ylmethyl, 2,3-dihydro-1-benzofuran-5-ylmethyl, chroman-6-ylmethyl, chroman-7-ylmethyl, 1H-indol-5-yl, 1H-indazol-5-yl, 1,2,3,4-tetrahydro-quinolin-6-yl or 2,3-dihydro-benzo[1,4]dioxin-6-ylmethyl, each of which is substituted with from 0 to 2 substituents independently chosen from hydroxy, halogen, C₁-C₂ alkyl and C₁-C₂alkoxy.

16. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein R₄ is benzo[1,3]dioxol-5-ylmethyl or 2,3-dihydro-benzo[1,4]dioxin-6-ylmethyl.

17. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein Ar represents phenyl substituted with from 0 to 4 substituents independently chosen from hydroxy, halogen, amino, cyano, nitro, -COOH, -CONH₂, -SO₂NH₂, oxo, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, C₁-C₄alkyl, C₁-C₄alkoxy, mono- and di-(C₁-C₆)alkylamino, C₁-C₄alkanoyl, C₁-C₂sulfonate, C₁-C₂alkylsulfonyl, C₁-C₂alkylsulfinyl, C₁-C₄alkylthio, C₂-C₄alkanone, C₁-C₄alkylester, C₁-C₄alkanoyloxy, C₁-C₂alkoxycarbonyl and C₁-C₂alkylcarboxamido.

18. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein Ar represents phenyl substituted with from 0 to 2 substituents independently chosen from hydroxy, halogen, amino, cyano, -COOH, -CONH₂, C₁-C₂ haloalkyl, C₁-C₂haloalkoxy, C₁-C₂alkyl, mono- and di-(C₁-C₂alkyl)amino, C₁-C₂alkoxy, C₁-C₂alkanoyl and C₁-C₂alkoxycarbonyl.

19. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein Ar represents phenyl fused to a 5- to 7-membered saturated or partially unsaturated ring having 0, 1 or 2 ring atoms independently chosen from N, O and S with remaining ring atoms being carbon, and wherein the phenyl fused to a 5- to 7-membered ring is substituted with from 0 to 4 substituents independently chosen from hydroxy, halogen, amino, cyano, -COOH, -CONH₂, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, C₁-C₂alkyl, mono- and di-(C₁-C₂)alkylamino, C₁-C₂alkoxy, C₁-C₂alkanoyl and C₁-C₂alkoxycarbonyl.

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20. (Currently Amended) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein Ar represents benzo[1,3]dioxol-5-yl, 2,3-dihydro-1-benzofuran-6-yl, 2,3-dihydro-1-benzofuran-5-yl, chroman-6-yl, chroman-7-yl, 1H-indol-5-yl, 1H-indazol-5-yl, 1,2,3,4-tetrahydro-quinolin-6-yl or 2,3-dihydro-benzo[1,4]dioxin-6-yl, each of which is substituted with from 0 to 2 substituents independently chosen from hydroxy, halogen, C₁-C₂ alkyl and C₁-C₂alkoxy.

21. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein Ar represents benzo[1,3]dioxol-5-yl or 2,3-dihydro-benzo[1,4]dioxin-6-yl.

22-23. (Cancelled).

24. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein R is morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, azetidiny, homopiperidinyl, homomorpholinyl, homopiperazinyl or thiomorpholinyl, each of which substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, COOH, C₁-C₃alkyl and C₁-C₃alkoxy.

25. (Original) A compound or pharmaceutically acceptable form thereof according to claim 2, wherein:

R₂ is propyl, butyl, pentyl or 3-methylbutyl;

R₃ is hydrogen;

R₅ is hydrogen;

R₆ is hydrogen, methyl or ethyl; and

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Ar represents phenyl fused to a 5- to 7-membered saturated or partially unsaturated ring having 0, 1 or 2 ring atoms independently chosen from N, O and S with remaining ring atoms being carbon, and wherein the phenyl fused to a 5- to 7-membered ring is substituted with substituted with from 0 to 2 substituents independently chosen from hydroxy, halogen, C₁-C₂ alkyl and C₁-C₂alkoxy.

26-27. (Cancelled).

28. (Currently Amended) A compound or pharmaceutically acceptable form thereof according to ~~claim-26~~claim 25, wherein R₄ is:

- (i) benzyl substituted with from 0 to 2 substituents independently chosen from hydroxy, halogen, amino, cyano, -COOH, -CONH₂, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, C₁-C₂alkyl, mono- and di-(C₁-C₂)alkylamino, C₁-C₂alkoxy, C₁-C₂alkanoyl, and C₁-C₂alkoxycarbonyl; or
- (ii) benzyl fused to a 5- to 7-membered saturated or partially unsaturated ring having 0, 1 or 2 ring atoms chosen from N, O, and S with remaining ring atoms being carbon, wherein the benzyl fused to a 5- to 7-membered ring is substituted with from 0 to 2 substituents independently chosen from hydroxy, halogen, C₁-C₂alkyl and C₁-C₂alkoxy.

29. (Original) A compound or pharmaceutically acceptable form thereof according to claim 25, wherein:

- R₁ is hydrogen, hydroxy, halogen, amino, cyano, trifluoromethyl, pentafluoroethyl, difluoromethyl, trifluoromethoxy or difluoromethoxy; and
- R is morpholinyl, piperazinyl, piperidinyl, pyrrolidinyl, azetidiny, homopiperidinyl, homomorpholinyl, homopiperazinyl or thiomorpholinyl, each of which substituted with from 0 to 3 substituents independently chosen from hydroxy, halogen, amino, cyano, COOH, C₁-C₃alkyl and C₁-C₃alkoxy.

30. (Cancelled).

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31. (Original) A compound or pharmaceutically acceptable form thereof according to claim 29, wherein R₄ is

- (i) benzyl substituted with from 0 to 2 substituents independently chosen from hydroxy, halogen, amino, cyano, -COOH, -CONH₂, C₁-C₂haloalkyl, C₁-C₂haloalkoxy, C₁-C₂alkyl, mono- and di-(C₁-C₂)alkylamino, C₁-C₂alkoxy, C₁-C₂alkanoyl and C₁-C₂alkoxycarbonyl; or
- (ii) benzyl fused to a 5- to 7-membered saturated or partially unsaturated ring having 0, 1 or 2 ring atoms chosen from N, O, and S with remaining ring atoms being carbon, wherein the benzyl fused to a 5- to 7-membered ring is substituted with from 0 to 2 substituents independently chosen from hydroxy, halogen, C₁-C₂alkyl and C₁-C₂alkoxy.

32. (Original) A compound or pharmaceutically acceptable form thereof according to claim 1, wherein the compound exhibits an IC₅₀ of 500 nM or less in a standard *in vitro* C5a receptor-mediated chemotaxis or calcium mobilization assay.

33. (Original) A compound or pharmaceutically acceptable form thereof according to claim 1, wherein the compound exhibits an IC₅₀ of 25 nM or less in a standard *in vitro* C5a receptor-mediated chemotaxis or calcium mobilization assay.

34. (Original) A compound or pharmaceutically acceptable form thereof according to claim 1, wherein the compound exhibits less than 5% agonist activity in a GTP binding assay.

35. (Original) A pharmaceutical composition comprising at least one compound or pharmaceutically acceptable form thereof according to claim 1, in combination with a physiologically acceptable carrier or excipient.

36. (Original) A method for inhibiting signal-transducing activity of a cellular C5a receptor, comprising contacting a cell expressing C5a receptor with at least one

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compound or pharmaceutically acceptable form thereof according to claim 1, and thereby reducing signal transduction by the C5a receptor.

37. (Original) A method according to claim 36, wherein the cell is contacted *in vivo* in an animal.

38. (Original) A method according to Claim 37, wherein the animal is a human.

39. (Original) A method of inhibiting binding of C5a to C5a receptor *in vitro*, the method comprising contacting C5a receptor with at least one compound or pharmaceutically acceptable form thereof according to claim 1, under conditions and in an amount sufficient to detectably inhibit C5a binding to C5a receptor.

40. (Original) A method of inhibiting binding of C5a to C5a receptor in a human patient, comprising contacting cells expressing C5a receptor with at least one compound or pharmaceutically acceptable form thereof according to claim 1, in an amount sufficient to detectably inhibit C5a binding to cells expressing a cloned C5a receptor *in vitro*, and thereby inhibiting binding of C5a to the C5a receptor in the patient.

41. (Original) A method for treating a patient suffering from rheumatoid arthritis, psoriasis, cardiovascular disease, reperfusion injury, or bronchial asthma comprising administering to the patient a C5a receptor modulatory amount of a compound or pharmaceutically acceptable form thereof according to claim 1.

42. (Original) A method for treating a patient suffering from stroke, myocardial infarction, atherosclerosis, ischemic heart disease, or ischemia-reperfusion injury comprising administering to the patient a C5a receptor modulatory amount of a compound or pharmaceutically acceptable form thereof according to claim 1.

43. (Original) A method for inhibiting C5a receptor-mediated cellular chemotaxis, comprising contacting mammalian white blood cells with a C5a receptor

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modulatory amount of a compound or pharmaceutically acceptable form thereof according to claim 1.

44. (Original) A method for localizing C5a receptor in a tissue sample, comprising:

- (a) contacting the tissue sample containing C5a receptor with a detectably labeled compound according to claim 1 under conditions that permit binding of the compound to C5a receptors; and
- (b) detecting the bound compound.

45. (Original) A packaged pharmaceutical preparation, comprising:

- (a) a pharmaceutical composition according to claim 35 in a container; and
- (b) instructions for using the composition to treat a patient suffering from rheumatoid arthritis, psoriasis, cardiovascular disease, reperfusion injury, or bronchial asthma.

46. (Original) A packaged pharmaceutical preparation

- (a) a pharmaceutical composition according to claim 35 in a container; and
- (b) instructions for using the composition to treat stroke, myocardial infarction, atherosclerosis, ischemic heart disease, or ischemia-reperfusion injury.

47. (Original) A pharmaceutical composition according to claim 35, wherein the pharmaceutical composition is formulated as an injectible fluid, an aerosol, a cream, a gel, a pill, a capsule, a syrup, or a transdermal patch.

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